

Applicants: Adams et al.
Application No. 10/591,369
Amendment and Response dated March 15, 2010
Reply to Office Action of November 13, 2009
Page 2

Amendments to the Claims:

This claim listing replaces all prior versions, and listings of claims in the application.
Please amend the claims as follows:

1. (Currently amended) A powdered formulation which is a freeze-dried mixture of a sensitive active material and an excipient comprising consisting of:
~~from 0.01 preferably from 0.1, more preferably from 0.5 to 50 % by wt of the sensitive active material,~~
~~from 50 to 99.99, preferably to 99.9, more preferably to 99.5 % by wt of the excipient, from 0.1 to 10% by wt of additive/stabilizer,~~
~~wherein at least from 0.1 to 50 % by wt of the mixture is in an amorphous state; wherein the excipient is crystalline, it is selected from the group consisting of a eutectic salt, glycine, mannitol and sorbitol; wherein where the excipient is amorphous, it is selected from the group consisting of glutamine, serine, a monosaccharide, a disaccharide, a trisaccharide, a polysaccharide, polyethylene glycols having a molecular weight of about 6000, a polyamino acid, poly-d-lactic acid, amorphous lactose, a polyethylene glycol having a molecular weight up to 1000, a polyglycan, a polysaccharide, a cyclodextrin, povidone, micro-fine cellulose, potato starch and a protein.~~
2. (Currently amended) A formulation according to claim 1, of ~~from 0.1, preferably from 0.5, more preferably from 1~~ to 50 % by wt of the freeze-dried mixture in an amorphous state.
3. (Currently amended) A formulation according to claim 1, comprising:
~~from 0.01, preferably from 0.1, more preferably from 0.5 to 50 % by wt of sensitive active material in an amorphous state,~~
~~from 50 to 99.99, preferably to 99.9, more preferably to 99.5 % by wt of excipient in crystalline state,~~

Applicants: Adams et al.
Application No. 10/591,369
Amendment and Response dated March 15, 2010
Reply to Office Action of November 13, 2009
Page 3

0 - 5 % by wt of excipient in an amorphous state.

4. (Currently amended) A formulation according to claim 1, comprising:
from 0.01, ~~preferably from 0.1, more preferably from 0.5~~ to 50 % by wt of sensitive active material in a crystalline state,
from 50 to 99.89, ~~preferably to 99.8, more preferably to 99.4~~ % by wt of excipient in crystalline state, and
0.1 - 5 % by wt of excipient in an amorphous state.

5. (Currently amended) A formulation according to claim 1, comprising:
from 0.01, ~~preferably from 0.1, more preferably from 0.5~~ to 25 % by wt of an amorphous or a crystalline state of sensitive active material,
from 75 to 99.49, ~~preferably to 99.4, more preferably to 99~~ % by wt of a crystalline state excipient, and
0.5 - 5 % by wt of excipient in an amorphous state.

6. (Previously presented) A formulation according to claim 1 in which a saccharide is used to provide an excipient in an amorphous state.

7. (Previously presented) A formulation according to claim 1 in which a sugar alcohol is used to provide an excipient in a crystalline state.

8. (Currently amended) A formulation according to claim 1 wherein the formulation additionally comprises from 0.1 to 10% by wt (~~preferably from 1 to 10% by wt~~) of additive/stabilizer.

Applicants: Adams et al.

Application No. 10/591,369

Amendment and Response dated March 15, 2010

Reply to Office Action of November 13, 2009

Page 4

9. (Previously presented) A formulation as defined in claim 8 wherein the additive/stabilizer is an antioxidant, a free radical scavenger and/or a Maillard reaction suppresser.

10. (Previously presented) A formulation according to claim 1 wherein the sensitive active material is a labile organic and/or inorganic molecule, a biopolymer, a polypeptide, protein, enzyme, hormone, vitamin, antibiotic, polysaccharide, lipid, killed or live whole live cell.

11. (Previously presented) A formulation according to claim 10 wherein the sensitive active material is a virus (including phage), bacterium, fungus and/or eukaryote.

12. (Previously presented) A formulation according to claim 1 which has a stable crystalline/amorphous matrix.

13. (Previously presented) A formulation according to claim 1 which has a substantially reduced the hygroscopicity.

14. (Currently amended) A formulation according to claim 1 which has a hygroscopicity of less than 5% by weight, ~~preferably less than 3% by weight, more preferably less than 2% by weight,~~ wherein the hygroscopicity is measured by the percentage increase in the weight of the formulation after 8 hours in a 75% relative humidity environment.

15. (Previously presented) A dosage form comprising a formulation according to claim 1.

16. (Previously presented) A dosage form according to claim 15 which is a container which comprises the formulation or an article which has been formed from the formulation.

Applicants: Adams et al.
Application No. 10/591,369
Amendment and Response dated March 15, 2010
Reply to Office Action of November 13, 2009
Page 5

17. (Withdrawn) A method of preparing a powdered formulation which comprises forming a mixed solution of sensitive active material and excipient(s) containing:

from 0.01, preferably from 0.1, more preferably from 0.5 to 50 % by wt of the sensitive active material,

from 50 to 99.99, preferably to 99.9, more preferably to 99.5% by wt of the excipient, and freeze-drying the solution so that at least 0.1 % by wt of the freeze-dried blend is in an amorphous state.

18. (Withdrawn) A method according to claim 17 in which the active material freeze dries to a crystalline state and the mixed solution contains:

from 0.01, preferably from 0.1, more preferably from 0.5 to 50 % by wt of sensitive active material in amorphous state,

from 50 to 99.99, preferably to 99.9, more preferably to 99.5% by wt of excipient in crystalline state,

0.1 - 5 % by wt of excipient which freeze dries to an amorphous state.

19. (Withdrawn) A method according to claim 17 in which the active material freeze dries to an amorphous state and the mixed solution contains:

from 0.01, preferably from 0.1, more preferably from 0.5 to 50 % by wt of sensitive active material in crystalline state,

from 50 to 99.89, preferably to 99.8, more preferably to 99.4% by wt of excipient in crystalline state,

0 - 5 % by wt of excipient which freeze dries to an amorphous state.

20. (Withdrawn) A method according to claim 17, in which the mixed solution contains:

from 0.01, preferably from 0.1, more preferably from 0.5 to 25 % by wt of amorphous or crystalline state of sensitive active material,

Applicants: Adams et al.
Application No. 10/591,369
Amendment and Response dated March 15, 2010
Reply to Office Action of November 13, 2009
Page 6

from 75 to 99.49, preferably to 99.4, more preferably to 99% by wt of crystalline state excipient, 0.1 - 5 % by wt of excipient which freeze dries to an amorphous state.

21. (Withdrawn) A method according to claim 17 in which a sugar is used to provide an excipient in amorphous state.
22. (Withdrawn) A method according to claim 17 in which a sugar alcohol is used to provide an excipient in crystalline state.
23. (Withdrawn) A method of medical treatment which method comprises supplying to a human or animal patient a therapeutically effective amount of a formulation according to claim 1.
24. (Withdrawn) A method of medical treatment which method comprises supplying to a human or animal patient a therapeutically effective amount of a dosage form according to claim 15.
25. (Withdrawn) A method of reducing the hygroscopicity of a freeze dried formulation which is a freeze-dried mixture of a sensitive active material and an excipient containing:
 - from 0.01 preferably from 0.1, more preferably from 0.5 to 50 % by wt of the sensitive active material, and
 - from 50 to 99.99, preferably to 99.9, more preferably to 99.5% by wt of the excipient, wherein the method comprises the step of including in the formulation at least 0.1 % by wt of a sensitive active material and/or an excipient in an amorphous state.
26. (New) A powdered formulation which is a shelf freeze-dried mixture of a sensitive active material and an excipient comprising:

Applicants: Adams et al.
Application No. 10/591,369
Amendment and Response dated March 15, 2010
Reply to Office Action of November 13, 2009
Page 7

from 0.01 to 50 % by wt of the sensitive active material,
from 50 to 99.99 % by wt of the excipient,
wherein at least 0.1 % by wt of the mixture is in an amorphous state.

27. (New) A formulation according to claim 1, wherein the formulation comprises from 0.1 to 50% by weight of the sensitive active material.

28. (New) A formulation according to claim 1, wherein the formulation comprises from 0.5 to 50% by weight of the sensitive active material.

29. (New) A formulation according to claim 1, wherein the formulation comprises from 50 to 99.9% by weight of the excipient.

30. (New) A formulation according to claim 1, wherein the formulation comprises from 50 to 99.5% by weight of the excipient.